TRANSVAGINAL ULTRASOUND MEASUREMENT OF ENDOMETRIAL THICKNESS AS A BIOMARKER OF ESTROGEN LEVEL IN POSTMENOPAUSAL WOMEN

Dissertation Submitted to

THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY

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CERTIFICATE

This is to certify that the dissertation titled **"Transvaginal ultrasound measurement of endometrial thickness as a biomarker of estrogen level in postmenopausal women"** is a bonafide work done by Dr.S.Anitha, Government R.S.R.M. lying in Hospital, Stanley Medical College to the Faculty of Obstetrics and Gynaecology, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (Obstetrics and Gynaecology) is a bonafide research work carried out by her under our direct supervision and guidance.

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CONTENTS

INTRODUCTION

Transvaginal ultrasound is a non invasive diagnostic tool commonly used to evaluate women with postmenopausal uterine bleeding. The ultrasound examination for endometrial pathology includes a measurement of endometrial thickness. In clinical studies, endometrial malignancy is uncommon in women with an endometrial thickness measurement less than 5 mm. This study specifically evaluates transvaginal ultrasound measurements of endometrial thickness in postmenopausal women. Because the endometrium contains estrogen receptors and responds to circulating estrogens, endometrial thickness constitutes a potential marker of estrogen status in postmenopausal women. To the extent that transvaginal ultrasound effectively measures the endometrial thickness and estrogen status, endometrial thickness measurements may be used as a biomarker for study of hormone – related malignancy, including breast, ovarian, endometrial and even colon cancer.

This study aimed to validate the transvaginal ultrasound measurement of endometrial thickness in postmenopausal women by demonstrating relationships between endometrial thickness measurements and risk factors known to be associated with estrogen exposure. As endometrial thickness measured by transvaginal ultrasound relates to the status of estrogen it was correlated with serum estrogen levels . Endometrial thickness assessment by transvaginal ultrasound is a simple non invasise method which indicates estrogen levels in postmenopausal women.

REVIEW OF LITERATURE

History of ultrasound

The word sonar stands for sound navigation and ranging. Sonar utilizes a frequency of 3.5 MHz to 10 MHz beyond the range of human audibility. Ultrasound travels at a speed of 1560m/s in human tissue.

Sergal Sokolovin a Russian scientist is called the father of ultrasound. He emphasized the potential importance of Sonar in 1929.

Dr Karl Dussik in Austria applied ultrasound in medical diagnosis. In 1951, Wild and Reig reported a 90% accuracy in the diagnosis of cystic versus solid lesions of various organs using the scan technique.

In 1955, Ian Donald and Tom Brown designed the contact scanner. In 1961, Biparietal diameter was first measured by Ian Donald. About this time, Campbell began working with the growth patterns of fetus as measured by serial Biparietal diameter. In 1973, gray scale presentation was introduced. Piezo electric effect was first discovered by Pierre Curie in 1880.

Transvaginal ultrasound was first introduced in 1984 by Schwimmer S R and Lebovic J who used a 5 MHz, 13 mm transducer that was not specifically designed for vaginal work.

TRANSVAGINAL SONOGRAM

As the endometrial histology can be predicted with accuracy depending on the endometrial thickness and the internal architecture of the endometrium, it actually became “sonomicroscopy” wherein structures that are not discernable with the naked eye could be appreciated. Normal anatomy of the corpus uteri varies with age and parity. Length of the uterus in various age groups are:

Post pubertal	**Reproductive**	**Postmenopausal**
5 – 6 cm	7 – 8 cm	4 – 6 cm

The echogenecity and thickness of the normal endometrium will vary depending on the phase of the menstrual cycle. The normal endometrial thickness during the various phases of the menstrual cycle and during the perimenopausal period are given in the following table.

The thickness is measured in the long axis from basalis to the contralateral basalis. The measurement should include only tissue and not fluid.

Phase	Thickness mm
Menstrual	2 – 4
Early proliferative	4 – 6
Periovulatory	6 – 8
Secretory	8 – 14
Postmenopausal	4 – 8
Postmenopausal with hormone replacement therapy	4 – 10
Tissue insufficient for diagnosis	< 4 – 5

Not only the thickness, the echogenecity of the endometrium has certain specific charecteristics during the various phases of the menstrual cycle, thus enabling the histology of the endometrium to be evaluated with precision by examined with the transvaginal sonogram.

During the menstrual phase – the endometrium appears as an echogenic uninterrupted layer of 1 – 4 mm in the total anteroposterior width.

Grunfeld in 1991 has described three patterns in evaluating changes in the normal endometrium.

Pattern 1:

During the early proliferative phase the thickness is 2 – 4 mm. Endometrium functionalis is hypoechoic or isoechoic and endometrium basalis is somewhat echogenic.

Pattern 2:

Ultrasound appearance of late follicular endometrium is characterized by three layers. Trilaminar appearance or triple sign.

Middle layer represents the lumen of the endometrial cavity. The lumen is echogenic because the endometrium is coated with mucous that

acts as an interface and reflects ultrasound. Surrounding the lumen is the hypoechoic endometrium functionalis and the echogenic endometrium basalis. There is an increase in echogenecity from the basal layer upwards but the inner layer still has some hypoechogenic changes.

The endometrium functionalis is hypoechoic in the follicular phase because of the edematous stroma and the lack of arteriole invasion. The basalis is always echogenic because of increased edema and vascularity of the basalis. In a normal cycle, the endometrial thickness ranges from 6 – 12 mm in the late follicular phase. Endometrium grows in the late proliferative phase at a rate of 0.5 mm/ day.

The trilaminar appearance is characteristic of the periovulatory endometrium and was present in 92% of the late proliferative phase biopsies performed by Forrest et al. Transmission of the ultrasound and posterior acoustic enhancement are also characteristic of follicular phase and is present in 90% cases.

Pattern 3:

In the secretory phase, the whole endometrium from the basalis to lumen is very echogenic. The increase in echogenecity , most probably is due to increase in luteal phase secretions and vascularity. The increase in echogenicity is seen due to elevations in the progesterone but may precede the rupture of follicle. Cul de sac fluid is often seen behind the uterus on ultrasound and helps to confirm that ovulation has occurred. The endometrium achieves its greatest width in the mid secretory phase measuring upto 14 mm in width.

In post menopausal women the endometrial thickness is usually 4 – 8 mm. the American College of Obstetrics and Gynaecology has published a technical bulletin on gynaecologic ultrasound which sets additional guidelines for transvaginal ultrasound.

Below a cut off of 4-5 mm in anteroposterior thickness of the endometrium for women with postmenopausal bleeding, there may not be significant associated pathology. Less than 4 – 5 mm or a thin pencil line echo is usually associated with tissue insufficient for diagnosis.

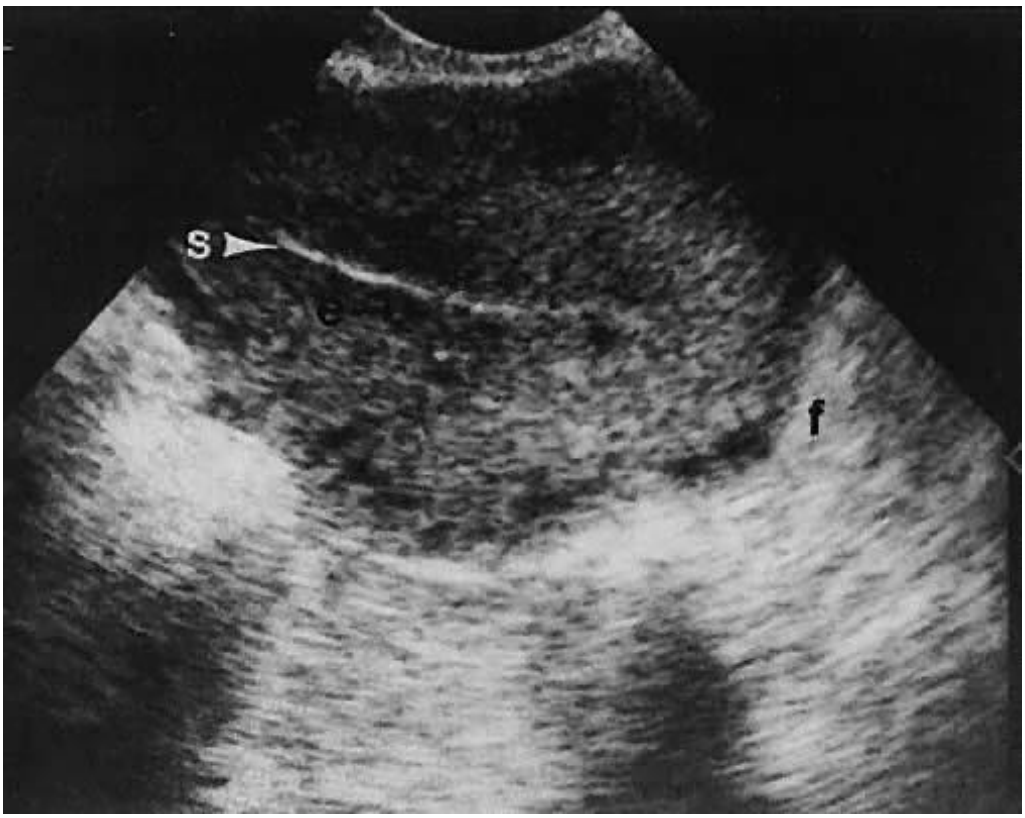
Those more than 5 mm may need endometrial sampling. Thus transvaginl sonogram maybe helpful in distinguishing patients with minimal endometrial tissue caused by postmenopausal atrophy and patients with significant endometrial tissue or polyps and are in need of further evaluation.

Transvaginal ultrasound of the pelvis is a highly reliable method for detecting endometrial cancer. In patients with postmenopausal bleeding, if the thickness of the endometrium is uniformly 5 mm or less, the probability of endometrial cancer is less than 1%. Sampling of the endometrium must be performed if there is diffuse thickening of the whole endometrium or focal thickening of part of the endometrium measuring 5 mm or more. The combination of abnormal vaginal bleeding and an endometrial thickness 5 mm or greater is 92% sensitive and 57% specific for endometrial cancer.

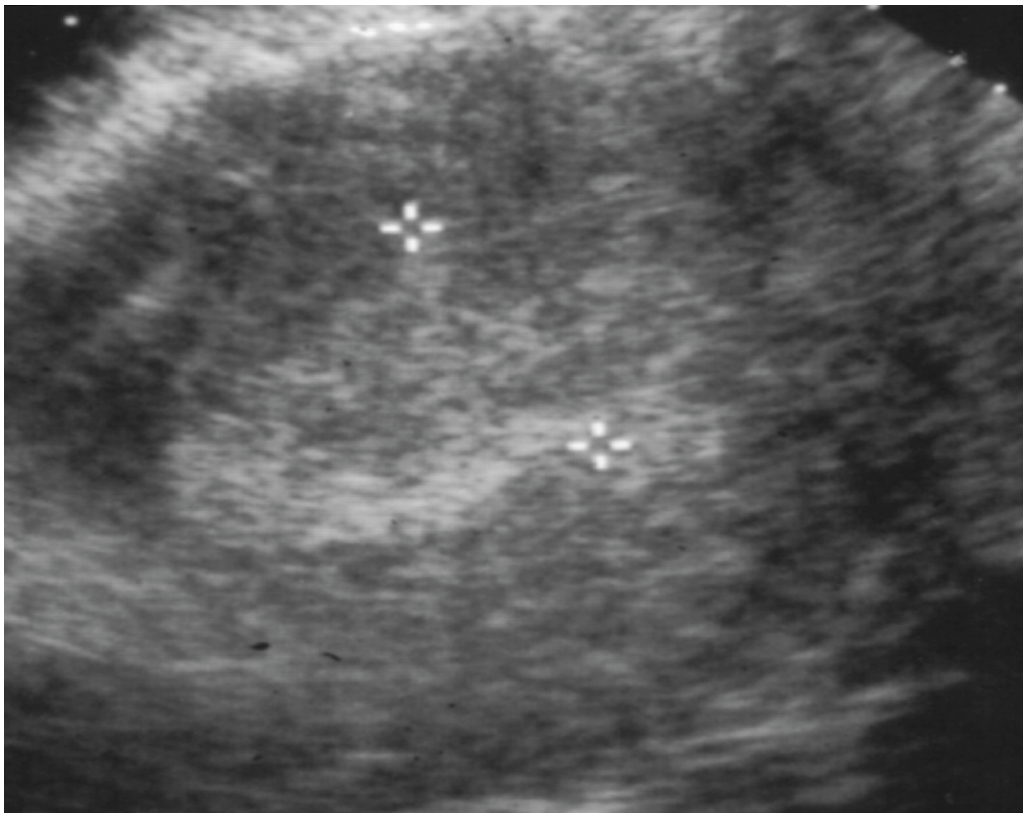
Transvaginal ultrasound may indicate the type of abnormality seen within the endometrium—for example, endometrial hyperplasia, polyps, or carcinoma. Classically, endometrial hyperplasia affects the entire endometrium and results in widening of the endometrium. The endometrial hyperplasia has a cystic lace-like appearance on ultrasound. Endometrial polyps manifest as focal areas of endometrial thickening,

and the stalk of the polyp may be seen if sufficient fluid is present in the endometrial cavity. Endometrial carcinoma may occur in the form of a polyp, within endometrial hyperplasia, or as a heterogeneous endometrial mass with a widened irregular cavity. Pathological confirmation of the histology is needed in all cases, as the ultrasound appearances overlap considerably. Endometrial biopsy is performed if the endometrial cavity is irregular, the endometrium has diffuse or focal widening greater than 5 mm, or if the whole endometrium has not been adequately assessed.

Transvaginal ultrasound may also identify ovarian pathology, including polycystic ovaries in younger women and ovarian tumours secreting oestrogens, causing abnormal vaginal bleeding. The ovaries are atrophic in most postmenopausal women and cannot be identified on ultrasound in up to 20% of women.



NORMAL ENDOMETRIAL LINING



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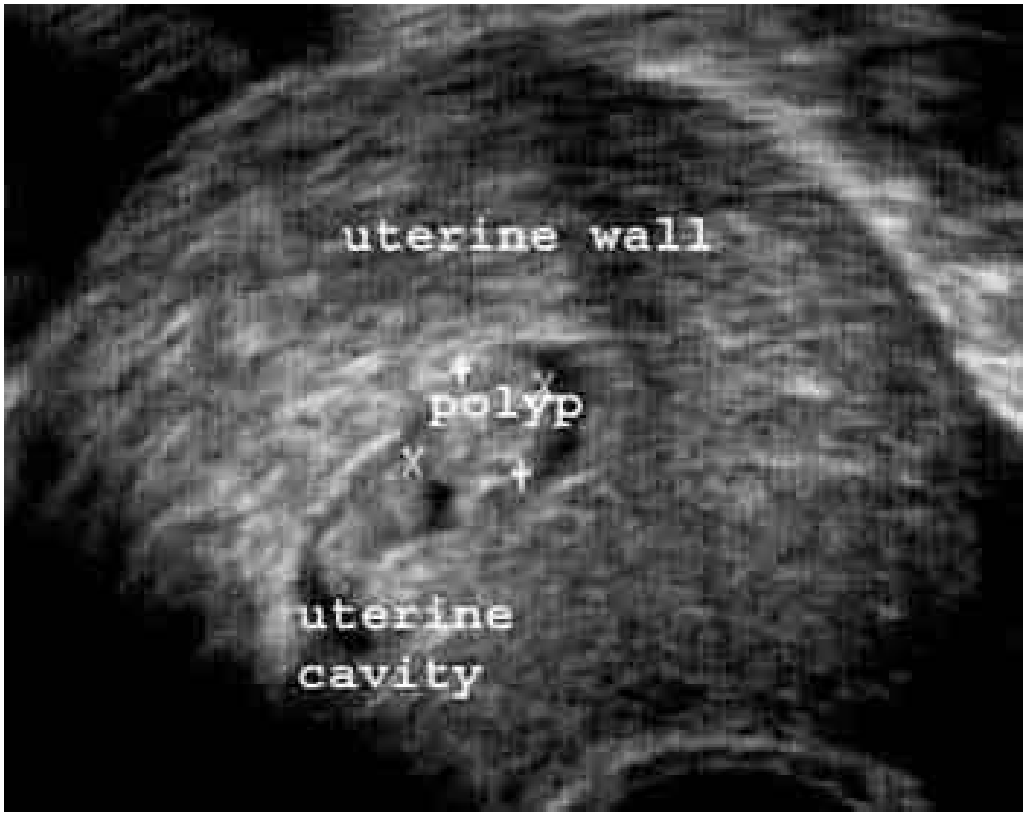
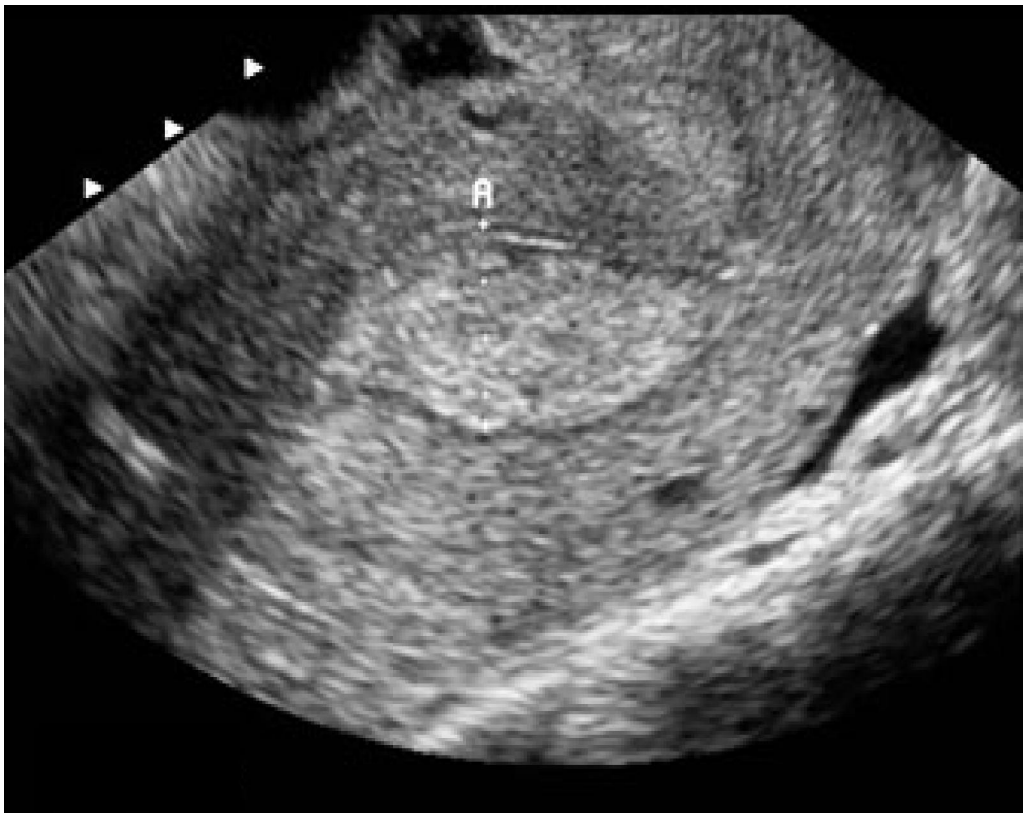


ENDOMETRIAL POLYP



ENDOMETRIAL CARCINOMA

In patients with endometrial carcinoma invasion into the myometrium can be determined. Loss of the subendometrial halo, consisting of compact myometrium is the first ultrasonic feature of invasion.

With more advanced myometrial invasion a distinct tumour – myomtrial interface can be visualized. Schoenfeld et al measured invasion from the endometrial lumen to the most distant tumor interface. This measurement divided by the total thickness of the uterine myometrium or the total anteroposterior uterine distance is divided by the total endometrial width. If this ratio exceeds 30%, myometrial invasion is suspected.

According to the latest FIGO classification, the depth of myometrial invasion distinguishes stage IB of endometrial cancer from stage IC. Gordon et al determined preoperative assessment of myometrial invasion by transvaginal sonogram in a group of 25 patients with histologically proven endometrial cancer and found that in 85% cases, transvaginal sonogram correctly predicted the depth of myometrial invasion within 15% of the actual measurement.

Transvaginal sonogram was accurate in 16 cases over diagnosis in 3 cases. Therefore sensitivity of transvaginal sonogram in detecting deep invasion was 100%, specificity more than 80% and accuracy 84%.

Cacciatore et al used preoperative ultrasonogram to stage 93 patients with endometrial cancer and were able to predict correctly myometrial invasion I 80%. Sonographic staging was accurate in 90% cases.

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Procedure of transvaginal sonogram:

Until recently, the primary method for detecting gynaecologic pathology was bimanual pelvic examination, with confirmatory or additional information supplied by transabdominal ultrasound.

Despite technical advances, transabdominal ultrasound imaging of the female reproductive tract was limited by attenuation of the sound beam by tissues of the anterior abdominal wall, distended urinary bladder, precluding the use of high frequency transducers (5 MHz) and the inability to correlate areas of visible pathology with direct palpation. Image resolution has improved dramatically with the introduction of transvaginal sonogram. The transducer is closer to the pelvic organs, higher frequencies can be used, reducing attenuation of the sound beam resulting in improved overall image quality.

Descriptions of the endometrium on ultrasound examination include global thickening, heterogeneity, thickening, focal areas of thickening, fluid collections, increased vascularity and myometrial associated findings such as myometrial cysts, and submucosal fibroids. After menopause, endometrial thickening may reflect proliferative

endometrium, cystic hyperplasia, complex hyperplasia, atypical hyperplasia, or carcinoma of the endometrium. Ultrasound evidence of thickened endometrium may also indicate structural abnormalities such as a uterine septum, submucous myomas, polyps, or adenomyosis. Ultrasound technology, by identifying vascular flow, now allows differentiation of polyps from other abnormalities. Increased vascularity and fluid accumulation in association with endometrial thickening are cause for greater concern than other findings.

Patient preparation:

Patient is informed about the procedure. She is asked to empty the bladder completely. This contributes greatly to patient comfort and acceptance of the technique. The best position is the dorsal position employed for vaginal examination. A transabdominal ultrasound is done prior to the vaginal study to exclude large masses and if the uterus is more than 19 cms, as in such conditions the vaginal study will be suboptimal due to its limited field of view. In all other cases, trans vaginal sonogram can be performed in lieu of abdominal scanning.

Transducer preparation:

Vaginal transducers are between 5 – 7.5 MHz in frequency. The size of the sector image is usually between 90- 115 degrees. The image is produced from an end firing transducer or a transducer that is angled upto 30 degrees off axis. Focal zones range from 1 – 8 cm. The transducer should be covered by a condom filled with approximately 5 ml of ultrasonic gel. Condoms that contain spermicidal agents should be avoided in cases of infertility.

Additional gel may be applied to the outside of the condom prior to its insertion, but this should be omitted in cases of infertility. Following completion of examination, the transducer assembly should be immersed in disinfectant for 10 minutes.

Probe manipulation:

Uterine corpus is an important structure in transvaginal sonogram and serves as a useful anatomic landmark for targeted organ imaging. Transducer orientation is unique in vaginal scanning, with the longitudinal plane directed from the patient’s feet to her head. Transverse scans are obtained in a coronal plane by rotating the transducer 90 degrees counterclockwise. Adnexa are optimally imaged

by positioning the transducer somewhat obliquely towards the contralateral side.

Confusion can also occur because of the actual position of the ultrasound beam which is 90 degrees off axis from the image on the monitor. This results in the longitudinal images being displayed on the monitor in a 90 degrees counterclockwise rotation from their actual position.

Ultrasound transducers have a reference mark. With the reference mark pointing up, left side of the screen represents a cephalad orientation and the top of the screen represents the anterior abdominal wall. With this view, an anteverted uterus points up and to the left while a retroverted uterus points down and to the right.

Anatomic changes due to scanning with an empty bladder must also be considered when performing a vaginal ultrasound. The uterine fundus becomes much more anteverted. In addition the ovaries often change their position following bladder decompression.

Sliding test:

It may be helpful to place one hand on the patients lower abdomen while performing the transvaginal sonogram in an effort to optimally position the ovaries in the transducer's field of view. Also areas of focal tenderness can be elicited with the movement of the transducer. Transvaginal sonogram can also be used in the follow up of women on Tamoxifen therapy for breast cancer and women on hormonal replacement therapy after menopause.

Postmenopausal endometrium and estrogen levels:

Endometrial cancer is a disease that occurs primarily in postmenopausal women and is increasingly virulent with advancing age. The role of estrogen in the development of most endometrial cancers has clearly been established. Any factor that increases exposure to unopposed estrogen increases the risk for endometrial cancer.

Serum estrogen levels decreases in postmenopausal women. Endometrial thickness is considered as a marker for estrogen status in postmenopausal women which can be measured by a transvaginal ultrasound.

Literature review shows that postmenopausal patients with a thickened endometrium (>5 mm) have significantly higher rates of endometrial cancer than patients with normal endometria. Many institutions have adopted a measurement of ≤5.0 mm or less to exclude patients from the need of pathologic evaluation. However, concerns have been raised about using transvaginal ultrasound as the sole method of evaluating endometrial pathology when focusing only on endometrial thickness. Uterine fibroids, hypertension, diabetes, obesity, the dosage of hormone replacement therapy (HRT) and other gynecologic factors increase endometrial thickness.

The mechanism for this increase in endometrial thickness is thought to be related to increased levels of circulating or local estrogens. For instance, Gull et al reported that uterine fibroids were associated with increased endometrial thickness, which could be attributed to the estrogen and progesterone receptors within the fibroids. Obesity also contributes to lower blood sex hormone binding globulin levels, insulin resistance, diabetes and high blood pressure. As a result, there is a shared association between obesity and altered estrogen levels that is partly responsible for increased endometrial thickness.

Reports of the incidence or true effect of co-morbidities such as obesity and diabetes on endometrial thickness and endometrial pathology are limited and contradictory. In fact, Gull et al found that risk factors previously shown to be associated with an increased risk for endometrial cancer such as obesity, hypertension and diabetes mellitus, were not shown to influence endometrial thickness. Incongruities between the studies and the lack of data reported encouraged to determine the effect that confounding risk factors have on the endometrial thickness and subsequent endometrial pathology.

CHARACTERISTICS		**RELATIVE RISK**
Nulliparity		2-3
Late menopause		2-4
Obesity	21 - 50 lbs overweight	3
	>50 lbs overweight	10
Diabetes Mellitus		2.8
Unopposed estrogen therapy		4-8
Tamoxifen therapy		2-3
Atypical endometrial hyperplasia		8-29
HNPCC Syndrome		20

Other factors leading to long term estrogen exposure such as polycystic ovary syndrome and functioning ovarian tumors are also associated with an increased risk of endometrial cancer other medical conditions such as hypertension and hypothyroidism have been associated with endometrial cancer, but a causal relationship has not been confirmed.

The guideline of the Dutch Society of Obstetrics and Gynecology does, among many other guidelines, recommend that endometrium sampling is not indicated if transvaginal ultrasonography shows a double layer less than 5 mm. Therefore, histology was obtained when the endometrial thickness exceeded 4 mm. This might have led to verification bias, which occurs when verification of the diagnosis depends on the test under study. Information on the subsequent development of a malignancy in the women with reassuring results at first diagnoses was not obtained unless they had recurrent bleeding. It is important to realize that further assessment of the endometrium was only dependent on the findings at ultrasonography and not on other risk indicators assessed in the present study, such as obesity, diabetes, or

hypertension, thus limiting the impact of verification bias on other findings.

In the literature, the accuracy of a diagnostic test is commonly reported in terms of sensitivity, specificity, and likelihood ratios. When such parameters are used, the crucial underlying assumption is that these indices remain constant for patients with different clinical characteristics.A diagnostic test should decrease the posttest risk of the presence of endometrial cancer to a level of approximately 5%, not only when used in women with a low pretest change for atypical hyperplasia or a malignancy of the endometrium, but also in women with a high pretest change. In women with a negative test (eg, in those with endometrial thickness under a certain cutoff point), further invasive diagnostic procedures can be omitted.

First, the incidence of malignancy is higher in women with postmenopausal vaginal bleeding and obesity (18%) or diabetes (21%), compared with women without one of these risk factors (8.0%).

In obese women with diabetes, the incidence was as high as 29%. Second, in the absence of malignancy, symptomatic women with obesity and/or diabetes have thicker endometria than women without these risk factors. In women diagnosed with a malignancy, endometrial thickness did not differ between patients with or without risk factors. Thus, whereas the pretest probability for malignancy was higher, the potential of the test to reduce the posttest probabilities to less than 5% was very limited.

Previous reports on this topic are scarce. In a sample of 559 asymptomatic postmenopausal women with (33%) or without HRT, the current use of HRT was the most important factor associated with endometrial thickness. Others found increased endometrial thickness in asymptomatic obese postmenopausal women.

Van der Bosch et al, who reported a significant positive correlation between both weight (0.24, $P < .01$) and BMI (0.26, $P < .01$) and the endometrial thickness in postmenopausal women with vaginal bleeding or endometrial cells on cervical cytology smear.

It is not clear that diabetes and obesity are independent factors that affect the diagnostic accuracy of transvaginal ultrasonography, and a synergistic effect cannot be excluded. There has been a reported decrease in the accuracy of transvaginal ultrasonography in obese women with diabetes compared with obese women without diabetes, for a strong increase in the incidence of cancer, thus indicating an independent effect. However, because of the relatively small number of patients with combined risk factors in various study cohorts, definite conclusions on this topic cannot be drawn.

The relation between endometrial thickness and hypertension has been examined in asymptomatic women. After correction for weight, Serdar Serin et al, found no relation between hypertension and endometrial thickness.

Pardo et al showed that, in women with an endometrial thickness exceeding 7 mm, endometrial atrophy was present in 84% of the patients on nifedipine, compared with 41% of women not on antihypertensive drugs. They stated that a drug effect on the endometrium caused a false-

positive test in women on nifedipine comparable with the phenomenon described for tamoxifen.

Endometrial sampling is the ‘‘gold standard’’ for diagnosing abnormalities in the endometrial tissue of patients with PMB. Since the sensitivity of endometrial sampling has been estimated to range from 85% to 95%, there has been a growing trend toward using a noninvasive procedure, such as high-resolution transvaginal sonography (TVS), to measure the endometrial thickness and to classify cases as being at low or high risk for malignancy, thus avoiding unnecessary sampling (Taipale et al., 2004).

Trans-vaginal ultrasonography can reliably assess thickness and morphology of the endometrium and can thus identify a group of women with postmenopausal bleeding who have a thin endometrium and are therefore unlikely to have significant endometrial disease. This group may not require any further investigation unless there is a recurrence of the bleeding (WHO, 1996).

The recent Scottish intercollegiate guideline network (SIGN) recommends that a trans-vaginal ultrasound scan should be the first line

investigation (Fornander et al., 1989). It is conventional to measure the thickness of both endometrial surfaces together (double thickness) at the thickest point in the mid-sagittal view assuming that the endometrial morphology is consistent throughout (WHO, 1996).

Some authors have revealed a relationship between the TVS determined endometrial thickness and histopathological findings. However, cutoff values of endometrial thickness below which cancer can be excluded have varied considerably (Gupta et al., 2002 and Bruchim et al., 2004).

Karlsson et al. (2001) could not find any association between endometrial thickness and smoking, late menarche, or early menopause, but parity was the most important factor associated with endometrial thickness. On the other hand, Gull et al. (2001) found that parity had an influence on uterine width and significantly associated with uterine size but it had no association with uterine length and endometrial thickness**.**

There are several factors known to be associated with endometrial cancer, e.g. obesity, early menarche, nulliparity, infertility, late

menopause, diabetes mellitus, hypertension, and use of hormone replacement therapy (HRT) (Gull et al., 2001).

It is known that multiparity, smoking, late menarche and early menopause are inversely associated with the risk of endometrial carcinoma (Levi et al., 2003).

Several studies have shown that the risk of the development of endometrial cancer is associated with increased endometrial thickness. (Ylostalo et al., 2003), and it is correlated furthermore with serum estradiol in premenopausal women, but in postmenopausal women serum estradiol mostly originates from a conversion of estrone in adipose tissue.

The few studies that have examined the relationship between endometrial thickness and body mass index (BMI) in postmenopausal women have shown that these two factors are related significantly (Andolf et al., 2004**).** Some studies have indicated that central adiposity is a strong and independent risk factor for endometrial cancer. High body mass index and abdominal fat distribution correlate with increased endometrial thickness and bone mass (Douchi et al.,)

Pathological conditions:

Recent studies with transvaginal ultrasound suggest that this modality may be of use in detecting endometrial abnormalities like polyps, endometritis, hyperplasia and carcinoma Leiomyoma are seen as echo dense defects within the myometrium. They are typically so dense that shadowing is apparent distal to the fibroid. Endovaginal sonography offers the opportunity to visualize the relationship of the fibroid to the endometrial cavity.

Adenomyosis do not have clear orders and are less dense than leiomyomata. They do not shadow like fibroids and are commonly cystic. They are seen as mottling within the myometrium. They may present as a myometrial mass or if glands begin secreting as cystic structures within the inner myometrium.

Endometrial filling defects – endometrial polyps are seen as endometrial filling defects. Scanning for endometrial contour defects should be done in the follicular phase because the hypoechoic endometrium serves to contrast against echogenic masses. The presence of a filling defect is 70% sensitive and 95% specific when compared with hysterosalpingogram. (Blumenfeld and Turner 1996)

AIMS OF THE STUDY

1. To validate transvaginal ultrasonographic measurement of endometrial thickness as a biomarker of estrogen exposure in postmenopausal women.

2. To correlate serum estradiol levels with endometrial thickness.

3. To study association between endometrial thickness and risk factors associated with estrogen exposure.

MATERIALS AND METHODS

Study population – 150 postmenopausal women in the age group 50 to 70 years.

Study carried out in Government RSRM Hospital after Ethical committee clearance during the period January 2010 to October 2010.

Data Collection - A self administered baseline questionnaire done before ultrasound screening gave information on age, years since menopause, body weight, height and medical disorders like diabetes and hypertension.

After informed consent and clinical examination, endometrial thickness is measured in longitudinal axis with real-time ultrasonography with a 7.5MHz transvaginal transducer.

Serum estradiol levels are measured by chemiluminescent immunoassay method and correlated with endometrial thickness.

Selection Criteria:

Women with natural menopause, not on HRT.

Exclusion Criteria:

Women on current treatment for cancer, recent tamoxifen use, participation in another cancer screening or primary prevention study.

Method:

A 7.5 MHz transvaginal sector probe with phased array and end firing potential was used.

All the patients were asked to empty their bladder prior to the examination.

The probe was covered with a sterile sheath or condom containing the acoustic gel.

The scan was performed with the patient in a supine position.

The transducer was introduced into the posterior vaginal fornix.

The uterus was scanned in the long axis and coronal views with special emphasis on endometrium. The scanning of the uterus was done first in the sagittal plane from the fundus to the internal os. Regularity of the uterus noted. The length, anteroposterior measurements and transverse dimensions of the uterus were noted and endometrial volume calculated.

Anteroposterior measurements of endometrial thickness were taken from basalis to contralateral basalis in the long axis of the endometrium. Oblique semicoronal views should be avoided as this may cause the endometrium to appear thicker.

Uterine cavity was examined systematically in both the sagittal and coronal views for the presence of submucous fibroid polyps, endometrial polyps, adenomyosis and endometrial architecture.

If there is suspicion of endometrial carcinoma, evidence and extent of myometrial invasion when present was noted. Now the probe was angled to the right or left of the midline in the sagitttal plane to image the ovaries. The internal echotexture of the ovaries were also imaged and any abnormalities were noted.

The entire pelvis was additionally examined to rule out any other pathology.

The results of the transvaginal sonogram were interpreted as:

Normal endometrium

Thickened endometrium echo or abnormal endometrial architecture

Endometrial polyps

Pyometra

Endometrial carcinoma

Submucous fibroid

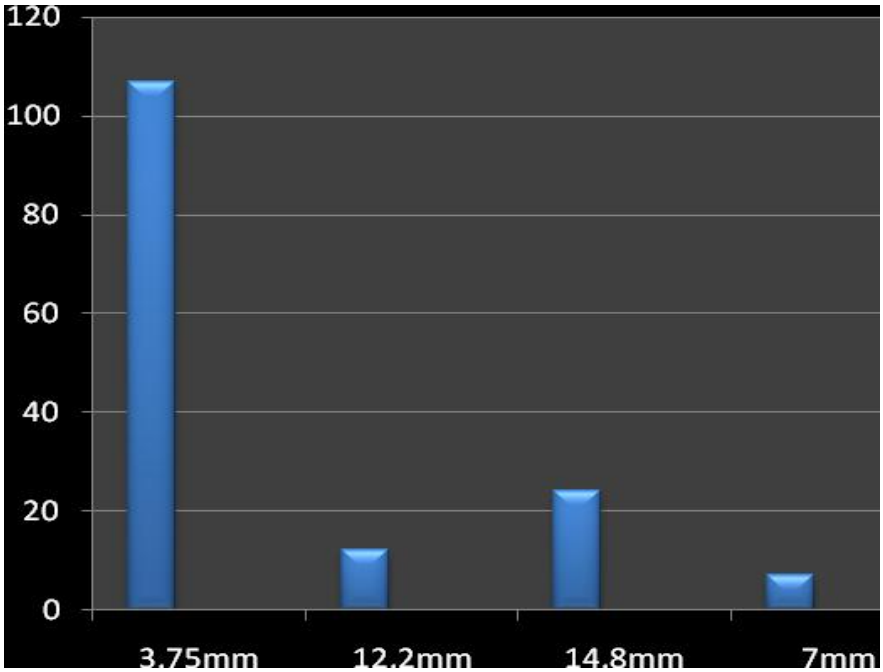
ANALYSIS AND OBSERVATIONS

TABLE 1: ENDOMETRIAL THICKNESS AND SERUM ESTROGEN LEVELS

Number of cases	Percentage of cases %	Endometrial thickness Mean thickness in mm	Serum estrogen levels Mean in pg/ml
107	71.3	3.75	14.6
12	8	12.2	18.25
24	16	14.8	32.45
7	4.7	16.7	38.36

Table 1: The endometrial thickness measurements in the study group and their respective serum estrogen levels are tabulated. The serum estrogen levels are high in patients with increased endometrial thickness.

Number of cases and endometrial thickness



107 Patients (71.3%) had mean endometrial thickness of 3.75mm.

12 Patients(8%) had mean endometrial thickness of 12.2mm.

24 Patients (16%)had mean endometrial thickness of 14.8mm

7 Patients(7%) had mean endometrial thickness of 16.7mm.

Among the 150 cases, 71.3% of cases had a mean endometrial thickness of 3.75 mm with mean serum estrogen levels of 14.6 pg/ml. 12% of the patients had a mean endometrial thickness of 12.2.mm with a mean estrogen level of 18.25 pg/ml. 24% of the patients had a mean endometrial thickness of 14.8 mm with mean estrogen level of 32.45 pg/ml.7% of the patients had a mean endometrial thickness of 16.7 mm with mean estrogen level of 38.36 pg/ml.

Thus patients with increased serum estrogen levels had endometrial thickness more than 5 mm.

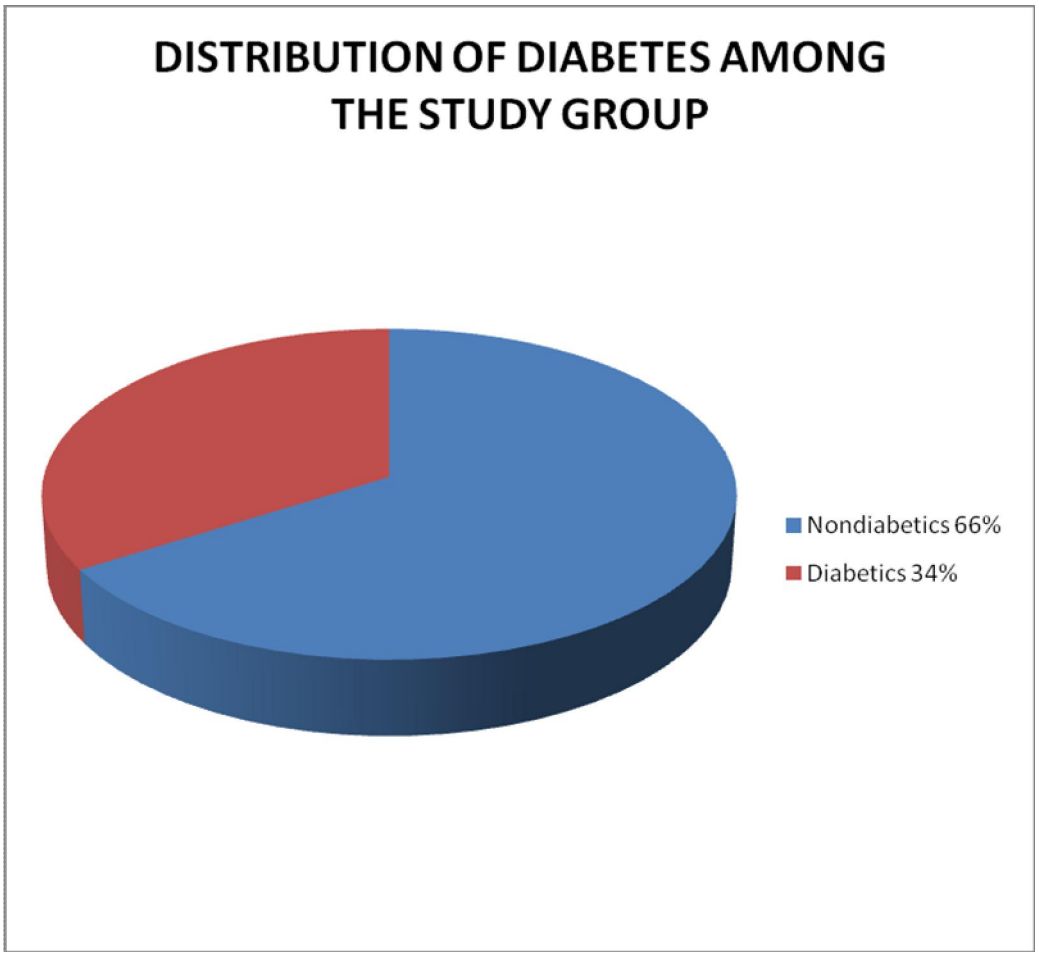
TABLE 2: RISK FACTORS AND ENDOMETRIAL THICKNESS

RISK FACTOR		**N=150**	**Percentage of cases %**	**ET>3mmm %**	**P value**
Diabetes	Ever	48	34	70	0.21
	Never	102	66	66.8	
Hypertension	Ever	27	18	69.8	0.04
	Never	123	82	65.9	

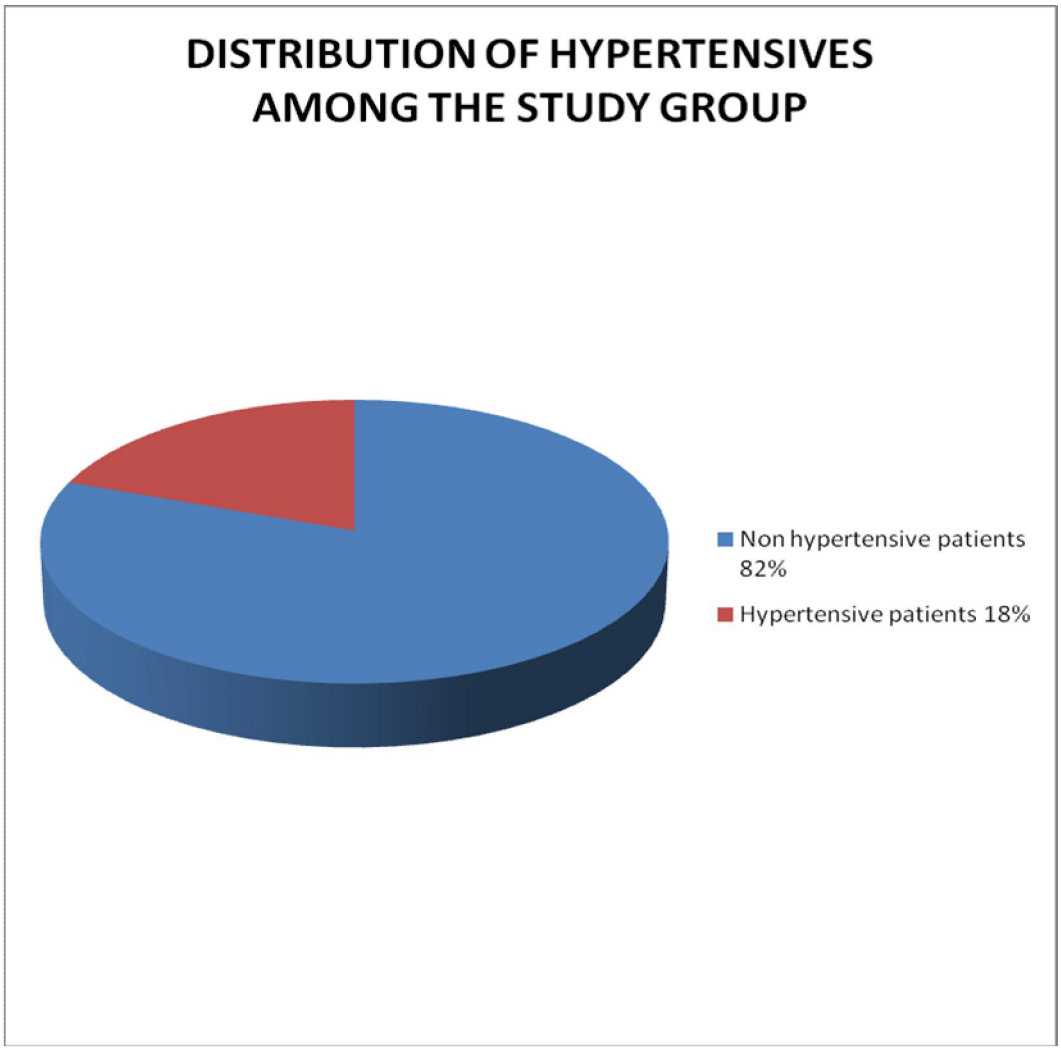
Table 2: The risk factors are diabetes and hypertension. The P value is statistically significant for the risk factor hypertension in the study group.

The number of patients with diabetes among the group was 48(34%) and P value was 0.21 correlating the endometrial thickness and the risk factor diabetes.

Among the 150 cases, 27patients (18%) had hypertension and P value was 0.04 correlating endometrial thickness and hypertension which was statistically significant.



66 % of patients were non-diabetics
34% of patients were diabetics



82 % of patients were non-hypertensives

18 % of patients were hypertensives

Table 3: AGE DISTRIBUTION AND ENDOMETRIAL THICKNESS

RISK FACTOR		n=150	ET>3 mm	P value
AGE	50-54	56	71.7	0.03
	55-59	39	66.9	
	60-64	33	62.8	
	65-70	22	58.7	

Table 3: The age of patients and the endometrial thickness measurements are tabulated above.

The endometrial thickness was correlated with the age of the patient and the P – value was 0.03, which was statistically significant**.** The lesser the age of the patient the more the endometrial thickness.

Table 4: AGE AT MENOPAUSE AND ENDOMETRIAL THICKNESS

RISK FACTOR		**n= 150**	**ET >3 mm %**	**P value**
AGE AT MENOPAUSE	< 40	24	60.3	0.06
	41– 49	43	70.2	
	>50	83	70	

The age at which menopause was attained and the endometrial thickness measurements were correlated. The P value was statistically significant.

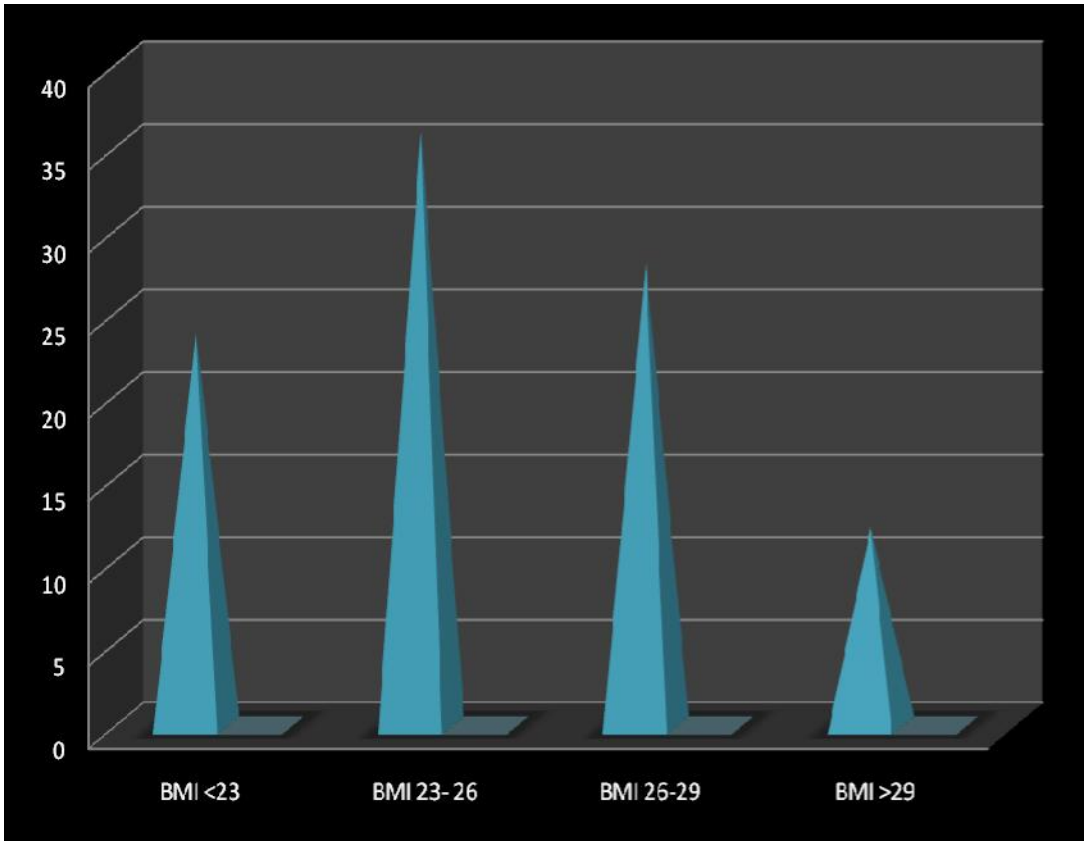
The age at which menopause was attained and the endometrial thickness was correlated among the patients. The endometrial thickness was more among the patients with late onset of menopause.

TABLE 5: BODY MASS INDEX AND MEAN ENDOMETRIAL THICKNESS

PERCENTAGE OF CASES n = 150	**BMI**	**MEAN ENDOMETRIAL THICKNESS IN mm**
24%	<23	3.4
36%	23 – 26	6.2
28%	26 - 29	11
12%	>29	13.4

Table 5: The body mass index distribution among the study group and the respective mean endometrial thickness are tabulated above. Increased endometrial thickness was found in patients with increased BMI.

BMI and endometrial thickness



24% with BMI <23 had endometrial thickness of 3.4mm
36% with BMI 23-26 had endometrial thickness of 6.2mm
28% with BMI 26-29 had endometrial thickness of 11mm
12% with BMI >29 had endometrial thickness of 13.4mm

Body mass index – BMI was calculated using the QUETELET index. BMI = weight in kg/ height in cm^2 .

The patients were divided into four groups according to the BMI. 24% of the patients had BMI less than 23 with endometrial thickness of 3.4 mm. 36% of patients with BMI 23 – 26 had endometrial thickness of 6.2 mm. 28 % of patients with BMI 26 – 29 had endometrial thickness of 11 mm. 12 % of patients had a BMI of more than 29 and an endometrial thickness of 13.4 mm. Thus patients with increased BMI had increased endometrial thickness.

RESULTS

Table1: Endometrial thickness and serum estrogen levels

From the present study, 71.3% of patients with mean endometrial thickness of 3.75 mm had serum estrogen level of 14.6 pg/ml, 8% of patients with mean endometrial thickness 12.2mm had a serum estrogen level of 18.25pg/ml. 16% of patients had a mean endometrial thickness of 14.8mm and serum estrogen levels of 32.45pg/ml. 7% of patients had a mean endometrial thickness of 16.7mm and a serum estrogen level of 38.36pg/ml.

Thus estrogen levels are high in patients with increased endometrial thickness.

Table 2: Risk factors and Endometrial thickness

The risk factors studied were diabetes and hypertension. Among the study group34% were diabetics, and 18% were hypertensive. The endometrial thickness was statistically significantly higher ($p= 0.04$) in the hypertensives. In the diabetes the endometrial thickness was not statistically significant ($p = 0.21$).

Table 3: Age distribution and endometrial thickness

The endometrial thickness was correlated with the age of the patient, with younger patients having a thicker endometrium (p=0.03).

Table 4: Age at Menopause and endometrial thickness

The age at which menopause was attained and the endometrial thickness correlated among the patients. The endometrial thickness was more among the patients with late onset of menopause (p=0.06)

Table 5: Body Mass Index and Endometrial thickness

24% of patients had BMI less than 23, 36% had a BMI of 23 to 26, 28 % patients had a BMI of 26 to 29 and 12% had a BMI more than 29. Increased endometrial thickness was found in 40% of the patients with increased BMI.

DISCUSSION

To validate transvaginal ultrasound measurement of endometrial thickness as a surrogate marker of estrogen status, in the present study the association between endometrial thickness and factors known to be associated with estrogen status in postmenopausal women were studied. From the present study a strong and consistent association between endometrial thickness and factors reflecting estrogen exposure was observed. Other studies have described similar associations involving endometrial thickness, diabetes hypertension, and BMI.

Studies about serum estrogen levels and endometrial thickness and which correlate with present study are:

1)Postmenopausal serum estradiol determination and endometrial thickness-Angel Cho and Chiehuan Ed Hsu et al.In this study,patients with less endometrial thickness had mean estrogen level of about 15.75 pg/ml which is consistent with the present study.5% of the patients in that study had endometrial carcinoma with mean endometrial thickness of 18.8mm and serum estrogen level of 37.48pg/ml which correlates with the present study.

2)Endometrial thickness in postmenopausal women as a marker for estrogen exposure-2004; Hill and Martin study. The frequencies of endometrial thickness with serum estrogen levels were 69% had mean estrogen level of 13.8 pg/ml,6% with 19.25 pg/ml,21% with 30.2pg/ml,and 4% with 39.6pg/ml. These results are consistent with the present study.

3) Judd and Frumer study-Origin of serum estrodiol in postmenopausal women.Among the study group 69% of the patients had serum estrogen levels of 16.75pg/ml with thinner endometrium.

In postmenopausal women not receiving HRT, serum estrogen concentrations increase with body weight due to peripheral aromatization of ovarian and adrenal androgens in adipose tissue.

Studies which corelate endometrial thickness and BMI are

1)Katanozaka and Douchi study-Relationship between BMI and transvaginal ultrasound endometrial thickness in postmenopausal women.The frequencies of thicker endometrium according to body mass index quartile (<23 ,23-26,26-29,>29) are 55.2%,66.1% ,69.7%,and

76.7%.Thus patients with increased BMI had increased endometrial thickness which is consistent with the present study.

2)Andolf and Aspenberg study(1993)-Ultrasonic thickness of the endometrium correlated to body weight in postmenopausal women.According to this study the distribution of thicker endometrium among the BMI quartiles were 4.2mm,7mm,12.8mm,and 14.6mm,which is consistent with the present study.

3)Van den Bosch et al-Age, weight, body mass index and endometrial thickness in postmenopausal women. In this study, age of the patient, weight, body mass index were tabulated against endometrial thickness. The lesser the age of the patient the more is the endometrial thickness which correlates with the present study. This study reported a significant positive correlation between body weight (0.24,$P<0.01$), BMI (0.26,$P<0.01$) and endometrial thickness. Thus the present study correlates with the above study.

The risk factors like diabetes and hypertension associated with increased endometrial thickness are correlating with studies like Matela et al, Salmi et al and Diaz studies which found association between risk factors like Hypertension, Diabetes and endometrial thickness.

Likewise other sources of information support associations involving endometrial thickness, age, uterine fibroids, hypertension and diabetes. Decreasing endometrial thickness with increasing age and increasing duration since menopause may reflect age and menopause related declines in ovarian function and blood estrogen levels. Like endometrium, uterine fibroids may contain estrogen and progesterone receptors. Hypertension and diabetes are endometrial cancer risk factors. Obesity, especially central obesity, contributes to lower blood sex hormone binding levels, insulin resistance and high blood pressure. A shared association with obesity and altered estrogen status explains, at least in part, the apparent effect of history of hypertension and diabetes on increased endometrial thickness.

In studies of women with postmenopausal bleeding and often endometrial hyperplasia, ultrasound measurements of endometrial thickness seems reproducible , with intra observer variation usually less than 5 % and inter observer variation in the range of 5 – 10 %. A large inter observer variation, relative to intra observer variation, suggests that operative skill and experience may affect the ultrasound measurement of

endometrial thickness. In contrast, fewer studies have evaluated the reproducibility of transvaginal ultrasound measurements of endometrial thickness in asymptomatic postmenopausal women, who have, on an average, atrophic endometria.

In clinical practice, the endometrial thickness measurement may be used to monitor women on HRT, to evaluate women with postmenopausal bleeding and to select women for more definitive procedures such as dilatation and curettage, hysteroscopy or endometrial biopsy. These latter procedures, in turn, constitute the gold standard for measuring endometrial thickness and recognizing pathologic states involving the endometrium. Recognizing these limitations, future applications using transvaginal ultrasound endometrial thickness measurements as a potential estrogen – related biomarker should consider the role of these more definitive diagnostic procedures in women with increased endometrial thickness.

Using information prospectively collected on a large sample of postmenopausal women recruited from the general community, we observed consistent and biologically plausible associations involving various risk factors and a single transvaginal ultrasound measurement of endometrial thickness. These findings validate, transvaginal ultrasound measurements of endometrial thickness as a measurement tool to validate endometrial thickness in postmenopausal women.

SUMMARY

1. From the study, serum estrogen levels co-related well with endometrial thickness in postmenopausal women.

2. The risk factors associated with estrogen exposure studied are age of the patient, age at menopause, diabetes, hyper tension and BMI. The statistically significant risk factors in the study group are age of the patient, age at menopause, hyper tension and increased BMI.

3. Thus transvaginal ultrasound measurement of endometrial thickness is a validate tool to diagnose endometrial pathology in postmenopausal women. It can be used as a first line procedure before other invasive diagnostic procedures. Thus endometrial thickness is a surrogate biomarker of serum estrogen level.

CONCLUSION

From this study, the endometrial thickness measurements correlated well with serum estrogen levels. Hence endometrial thickness in postmenopausal women is a surrogate marker for estrogen status.

The risk factors associated with estrogen exposure and endometrial thickness were also validated. P value less than o.o5 is statistically significant. From this study the risk factors statistically significant are age of the patient, age at which menopause was attained, history of hypertension and increased body mass index.

With the advent of transvaginal sonogram gynaecologists now have a simple outpatient method of studying the endometrium for detecting malignant lesions or their precursors at an earlier stage in postmenopausal women.

In postmenopausal women less than 5mm or thin pencil line endometrial echo is usually associated with atrophic endometrium. Endometrial carcinoma is diagnosed at an earlier stage by loss of the subendometrial halo which indicates myometrial invasion.

BIBLIOGRAPHY

1. Transvaginal ultrasound measurement of endometrial thickness as a biomarker of estrogen exposure –(2004) September – cancer epidemiological biomarkers – Sit A S, Hill L M, Martin J, Weissfeld J L

2. Role of transvaginal ultrasound or endometrial biopsy in the evaluation of the menopausal endometrium – Steven R Goldstein, July (2009) AJOG

3. Transvaginal sonography of the endometrium in postmenopausal women- Varner R E, Sparks T M, Cameron CD- Obstetrics Gymaecology, august 2009

4. The role of vaginal scan in the measurement of endometrial thickness in postmenopausal women- British Journal of obstetrics and Gynaecology- May 2008

5. Echographic monitoring of the endometrium with transvaginal probe in the menopause – D'amelio R, Perrone G

6. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding – Gull B, Carlsson S, Granberg S- March 2000, American journal of obstetrics and gynaecology

7. Rebleeding and endometrial growth in women with postmenopausal bleeding and endometrial thickness less than 5 mm managed by dilatation and curettage or ultrasound follow up – Epstein E, Valestin L- ultrasound obstetrics and gynaecology, 2001 November

8. Trnsvaginal ultrasonography for identifying endometrial pathology in postmenopausal women, Smith P, Heimer G

9. Endometrial scanning of the endometrium compared to cytology and histology in women with postmenopausal bleeding – Gynecological oncology 2006

10. Gohagen JK, prorok PC, Hayes RB, Kramer BS. The prostate, lung, colorectal and ovarian (PCLO) cancer screening trial. Control clinical trials 2000

11. Brash A, Wssmen A, Manor M, Milman D, Ben Arie A, Shoham Z. prospective evaluation of endometrial thickness as a predictor of pituitary down – regulation after gonadotropin releasing hormone analogue administration in an in vitro fertilization program. Fertil steril. 1998;69

12. Andolf E, Dhalander K, Aspenberg P, Ultrasonic thickness of the endometrium correlated to body weight in asymptomatic postmenopausal women. Obstet Gynecol 2003:84

13. Gull B, KarlssonB, Milsom I, Wikland M, Granberg S. Transvaginal sonography of the endometrium in a representative sample of postmenopausal women. Ultrasound obstrt gynecol 1996;7

14. Bar – Hava I, Perri T, Zahavi Zet al. Influence of hormone replacement therapy on postmenopausal pelvic organs. Climacteric 2001;4

15. Douche T, Yoshinaga M, Katanozaka . relationship between body mass index and transvaginal ultrasonographic endometrial thickness in postmenopausal women. Acta obstet Gynecol scand; 1998

16. Van den Bosch T, Vandendael A, Van Schoubroeck D, Lombard CJ, Wranz PA. age, weight, body mass index and endometrial thickness in postmenopausal women. Acta Obstet Gynecol Scand 1996

17. Hankinson S E, Willet WC, Manson JE et al. alcohol, height weight and adiposity in relation to estrogen and prolactin levels in postmenopausal women. J Natl Cancer Inst 1995

18. Judd HL, Shamonki IM, Frumar AM, Lagasse LD. Origin of serum estradiol in postmenopausal women. Obstet gynecol 1992

19. Speroff L, Glass RH, Kase NG. postmenopausal hormone therapy , chapter 18 in Speroff L, Glass RH, Kase NG editors Clinical Gynecologic endocrinology and infertility. 6th ed Philadelphia: Lippincott, Willials and Wilkins, 2004

20. Wang H, Wu X, Enguland K. Different expression of estrogen receptors alpha and beta in human myometrium and leiomyoma during the proliferative phase of the menstrual cycle and after GnRHa treatment. Gynecol Endocrinol 2001:15

21. Samadi AR, Le NC, Flanders WD, Boring JR III. Risk factors for self reported uterine fibroids. Epidemiology 1996;7

22. Parazzini F, Negri E, la Vecchia C. reproductive factors and risk of uterine fibroids. Epidemiology 1996:7

23. Faerstein E, Szklo M, Rosenstein N. risk factors for uterine leiomyoma: a practice based case control study. I African American Heritage, reproductive history, body size and smoking. Am J Epidemiology 2001

24. Gull B, karlsson B, Milsom I, Granberg S. factors associated with endometrial thickness and uterine size in a random sample of postmenopausal women. Am J ostet Gynecol 2001

25. Maatela J, Aromaaa A, Salmi T, Pohja M. the risk of endometrial cancer in risk groups of patients with diabetes and patients with hypertension. Cancer 1993

26. Diaz ME, hypertension and obesity. J Hum Hypertens 2002

27. Delisle MF, Villeneuve M, Boulvain M. measurement of endometrial thickness with transvaginal sonography: is it reproducible? J Ultrasound Med 1998

28. Yaman C, Ebner T, Jesacher K, Obermayr G, polz W. Reproducibility of three dimensional ultrasound endometrial volume measurements in patients with postmenopausal bleeding. Ultrasound Obstet Gynecol 2002; 19

29. Wolman I, Jaffa AJ, Sagi J, Hartoov J. Transvaginal ultrasonographic measurements of endometrial thickness: a reproducibility study. J Clin Ultrasound 1996.

30. Randelzhofer B, Prompeler HJ, Sauerbrei W. Value of sonomorphological criteria of the endometrium in women with postmenopausal bleeding: a multivariate analysis. Ultrasound Obstet Gynecol 2002

31. Gull B, Karlsson B, Milson I, Granberg S. Can ultrasound replace dilatation and curettage? A longitudinal study of postmenopausal bleeding and transvaginal measurement of the endometrium as predictors of endometrial cancer. Am J Obstet Gynecol 2003:188

32. Jacobson BH, Debock DH. Comparison of body mass index by self reported versus measured height and weight.Percep Mot Skills :2001:92

33. Endogenous Hormones and Breast Cancer Collaborative Group. Endogenous sex hormones and breast cancer in postmenopausal women: reanalysis of nine prospective studies. J Natl Cancer Inst 2002:94

PROFORMA

NAME: AGE: I.P NO:

D.O.A: RESIDENCE:

D.O.D:

MENSTRUAL HISTORY:

Age of menarche:

Bleeding: profuse/ moderate/ scanty

Menstrual cycles: regular/irregular /days

Dysmenorrhea: present/ absent

Intermenstrual bleeding:

Menopause: years

TREATMENT HISTORY:

EARLIER CONTRACEPTIVE HISTORY

ORAL CONTRACEPTIVE PILLS

INTRAUTERINE CONTRACEPTIVE DEVICES

OBSTETRIC HISTORY:

Married life parity living children

Last child birth sterilization

PAST HISTORY: Diabetes

Hypertension, Family history of Carcinoma

PERSONAL HISTORY:

PHYSICAL EXAMINATION:

General condition:

Nourishment:

Built:

Height:

Weight:

BMI:

PER ABDOMEN: PER SPECULUM EXAMINATION

VAGINAL EXAMINATION:

INVESTIGATIONS:

Serum estrogen level:

Blood sugar:

Blood urea:

Serum creatinine:

VAGINAL SONOGRAPHY:

Uterus:

Endometrial thickness:

Cervix:

Right ovary

Left ovary

CERTIFICATE FOR APPROVAL OF ETHICAL COMMITTEE

To

Dr.S.Anitha, PG in MD(OG)

Dear **Dr.S.Anitha, PG in MD(OG)**

The Institutional Ethics Committee reviewed and discussed your application for approval of the project entitled

"Transvaginal Ultrasound Measurement of endometrial thickness as biomarker for estrogen exposure"

The following members of the ethics committee were present at the meeting held on 28.01.2008 at the Council Hall, Stanley Medical College, Chennai-1 at 10.00AM

Dr.C.B.Tharani, Director of Pharmacology,
Madras Medical College, Chennai-3 - Chairman of the Ethics Committee
Dr.S. Chitra, Vice-Principal,
Stanley Medical College, Chennai – 1- Member Secretary of the Ethics Committee

MEMBERS

Dr.Jayanthi
Prof.of Medical Gastroenterology
Dr.Madhavan
Prof.of Pharmacology
Dr.E.Dhandapani
Prof.of Medicine
Dr.Sujatha Sridharan
Prof.of Paediatrics
Thiru.Pachaiappan,
Junior Administrative Officer,
Thiru.A. Senthil Manoharan,
Advocate

We approve the project to be conducted in its presented form.

The Institutional Ethics Committee/Independent Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

Yours sincerely,

Member Secretary,
Ethics Committee

MEMBER SECRETARY
ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE
CHENNAI-600 001.

MASTER CHART

Sl. No	Name I.P.No.	Age Parity	Menopause& Risk factor	Uterine size	Endometrial Thickness (mm)	Serum estrogen levels pg/ml	BMI
1.	Veeramma 9386	55,P5L4	2 yrs back	7x4.3x2.4	13	36.8	30
2.	Shankari 22960	50,P3L3	1yr HT	6x4.3x2.6 1.1x1.1	8	11.2	28
3.	Narasamma 10214	52	1yr DM	5.4x3.5x2.1	8.0	15.6	22
4.	Kandammal 10277	52,P6L6	8yrs	4x4.3x3.4	4	18.45	23
5.	Muniammal 10349	50,P5L3	3yrs	4.1x1.9x1.1	6	16.6	25
6.	Kuppammal 10977	47,P3L2	1yrs DM	4.6x4.2x3.3	8	35.6	31
7.	Andal 12187	50,P1L1	2yrs	4.7x2.5x2.8	8	21.5	26
8.	Kamatchi 11898	49,P4L4	2yrs	2.8x3x2.9	8	18.9	24
9.	Bhanumathy 11990	48,P2L2	11/2yrs DM	4.3x3.2x2.6	8	14.2	26
10.	Ranikutty 11501	48,P3L3	3yrs	4.7x3.3x2.0	8	14.8	21
11.	Kamala 6869	60,Nullipara	4yrs HT	9.4x4.7x4.3	16	16.6	24
12.	Muniamma 9497	54,P2L2	2yrs	3.5x2.6x1.2	2	10.6	27
13.	Rakayee 21865	49,P3L3	2yrs DM	4.2x1.2x1.6	3	26.6	25
14.	Shanthi 23793	52,P4L3	3yrs	4.2x2.6x1.2	2	16.8	22

15.	Kathammal 13897	50,P6L6	2yrs back HT	4.3x2.7x1.2	4	6.9	28
16.	Selvi 14901	49,P5L4	4yrs DM	5x2.2x1.2	5	8.65	24
17.	Sundari 13741	50,P2L1	3yrs	3.6x2.4x1.2	5	10.2	21
18.	Karupayee 8498	49,P4L2	3yrs HT	3.4x2.4x1.6	4	10.4	23
19.	Senthil 9430	49,P3L2	4yrs	4.2x2.1x1.8	4	14.8	23
20.	Sivapayee 16981	48,P2L3	4yrs DM	3.9x2.3x1.6	3	25.6	21
21.	Kalairasi 17914	49,P3L1	4yrs	3.6x3.2x1.1	5	14.6	32
22.	Laxmi Elumalai 7937	50,P6L6	2yrs	7.5x4.4x2.3	13	14.9	26
23.	Kuppammal 9966	57	10yrs	8.4x4.1x4.4	18	16.9	24
24.	Rajakumari 7891	51,P3L13	4yrs DM	4.3x2.7x1.2	1.2	12.2	20
25.	Kasthuri 7985	60,P3L3	9yrs	5x2.2x1.4	6	14.6	28
26.	Krishnaveni 12143	49,P2L12	2yrs	5x3.8x2.2	14	14.68	27
27.	Eswari 17149	47,P2L2	2yrs	4.1x2.7x1.1	3	39.36	31
28.	Kamatchi 17497	62,P2L2	12yrs	3.6x2.9x1.4	4	26.6	25
29.	Chittu 14923	60,P3L3	11yrs DM	3.9x1.8x1.6	5	6.6	22
30.	Pattu 16492	57,P8L6	8yrs	4.0x2.0x1.4	4	10.2	24

31.	Karumari 12492	56,P4L4	7yrs back HT	4.4x2.0x1.1	3	10.4	27
32.	Irumayet 17391	60,P6L5	8yrs	3.9x2.0x1.6	5	12.4	26
33.	Rani Jeyaram 12345	46,P8L6	2yrs DM	4.8x2.3x1.1	5	11.2	21
34.	Mariammal 7505	75,P3L3	30yrs	6.3x5.3x4.2	16	14.8	25
35.	Manjula 8909	54,P2L2	4yrs	5x3.2x2.4	10	36.28	30
36.	Angammal 12450	60,P4L4	6yrs DM	6.4x3.2x3.4	6	14.62	25
37.	Vasantha 7941	47,P4L4	2yrs	5.2x2.3x1.1	4	14.5	26
38.	Ambika 17641	51,P5L5	2yrs	4.8x2.8x1.2	5	12.6	28
39.	Sampoornam 12416	52,P2L1	6yrs HT	4.6x2.1x1.3	5	30.2	23
40.	Sornam 7916	53,P4L4	6yrs	4.0x2.5x1.4	5	12.6	20
41.	Mariamma 7841	57,P8L7	10yrs DM	6.4x2.3x1.1	10	15.2	24
42.	Revathy 17621	47,P6L6	2yrs DM	5.4x3.0x2.9	8	5.8	26
43.	Saroja 14594	48,P4L4	2yrs	4.1x1.1x2.1	5	39.6	30
44.	Pappa 13141	44,P2L2	1yrs	4.6x2.1x1.9	8	10.6	22
45.	Pappamma 7941	51,P5L4	6yrs HT	3.6x2.5x1.6	4	32.4	26
46.	Rajathy 13141	48,P3L3	4yrs DM	5.2x3.0x2.6	8	12.6	24

47.	Kuppamma 16131	52,P6L5	6yrs back HT	4.6x2.1x1.1	4	18.2	21
48.	Ponnatha 14842	54,P6L6	4yrs	4.8x3.1x2.6	11	34.4	23
49.	Ponnamma 1781	47,P5L4	2yrs DM	6.4x4.2x2.1	12	14.2	27
50.	Thirupura Sundari 15421	45,P1L1	2yrs DM	4.1x3.5x2.4	10	8.8	21
51.	Kasthuri 9299	42,P4L4	2 yrs DM	4.1x1.8x1.2	5	35.6	30
52.	Arasani 9298	45,P1L4	1yrs DM	6.4x7.8x2.8	9	12.6	28
53.	Chellamma 10215	42,P2L2	1yrs HT	4.1x2.4x2.5	9	34.2	22
54.	Devaki 9964	45,P1L1	8yrs	8.2x5.5x2.1	18	12.4	23
55.	Rani Rethnam 9301	45,P4L4	3yrs HT	4.1x3.3x2	9	16.6	25
56.	Rajam 9965	44,P5L5	1yrs DM	4.9x3.8x1.6	17	15.6	31
57.	Rani 10217	44,P2L2	2yrs	4.2x3.6x2.1	10	18.2	26
58.	Rani Renganath 10882	45,P3L3	2yrs DM	8.6x4.4x5.1	10	32.5	24
59.	Ruckmani 10972	48,P4L4	11/2yrs	6.8x3.5x2.0	11	16.2	26
60.	Jamuna 10979	43,P3L3	3yrs DM	6.2x5.3x4.2	16	12.2	21
61.	Elliammal 8580	43,P3L3	4yrs	4.6x2.4x1.6	8	12..4	24
62.	Radhamani 9293	53,P6L6	2yrs DM	8.4x5.3x2.6	16	14.6	27

63.	Rani 23214	44,P3L3	2yrs back DM	4.6x3.3x2.0	9	10.5	25
64.	Ruckmani 11212	48,P1L1	3yrs	8.1x4.7x4.2	27	10.6	22
65.	Guna 11903	47,P4L4	2yrs DM,HT	5.2x4.8x2.1	10	14.25	28
66.	Uma 12248	43,P2L2	4yrs	4.5x3.2x1.9	10	14.8	24
67.	Rani Shanmugam 11606	44,P2L2	3yrs	7.3x6.3x2.4	9	14.56	21
68.	Ahima Bee 11846	43,P3L3	3yrs HT	5.2x4.4x2.4	8	14.2	23
69.	Dhanalakshmi 10916	42,P4L4	4yrs	7.0x6.3x2.5	19	12.6	23
70.	Mallika 10208	43,P3L3	4yrs HT	4.7x3.8x2.0	10	31	21
71.	Rani Raghavan 1501	43,P3L3	4yrs DM	4.7x3.3x2	8	11.2	32
72.	Saraswathy 10807	44,	2yrs DM	7.9x3.2x2.3	13	10.6	26
73.	Nagammal 11460	44,P3L3	10yrs	6.5x3.9x4.6	8	16.8	24
74.	Thangammal 7931	50,P8L8	4yrs HT	6.6x3.9x4.6	10	16.2	20
75.	Chellammal 6279	50,P7L7	9yrs	8.9x3.8x2.4	9	15.1	28
76.	Vellammal 7938	44,P2L2	2yrs	6.4x3.2x2.4	10	30.5	27
77.	Alamelu 11458	54,P5L5	2yrs HT	9.1x8.1x3.4	23	12.45	31
78.	Rathinam 11463	42,P3L3	12yrs	7.5x4.0x4.2	10	12.9	25

79.	Suseela 11785	48,P3L3	11yrs back DM	8.4x4.0x3.2	8	14.6	22
80.	Ramamani 26215	44,	8yrs DM	8.9x4.9x5.8	18	16.3	24
81.	Ellammal 12094	42,P4L4	7yrs	5.1x4.2x2.6	8	18.8	27
82.	Syed Ali Fathima 12268	45,P3L3	8yrs HT	4.0x3.1x2.4	8	12.4	26
83.	Leela 74199	42,P3L3	2yrs HT	8.0x4.2x3.2	11	11.6	21
84.	Jeyammal 7520	44,P3L3	30yrs	10x5.1x3	10	31.2	25
85.	Velammal 7938	42,P2L2	4yrs	4.0x4.2x2.5	8	10.8	30
86.	Kuppammal Parthiban 11523	45,P2L2	6yrs DM	7.0x4.2x3.2	8	12.8	25
87.	Pattu 15187	43,P3L3	2yrs DM	5.1x4.2x2.5	7	12.2	26
88.	Rajakumari 6916	44,P4L4	2yrs	4.6x4.2x2.6	8	16.2	28
89.	Jamuna Bai 7918	43,P2L2	6yrs	6.8x3.5x2.4	16	9.8	23
90.	Santhanam 18431	54,P3L3	6yrs HT	6.4x5.2x4.3	20	12.4	20
91.	Murugammal 17341	47,P3L2	10yrs DM	5.4x4.3x3.24	8	13.5	24
92.	Vani 17324	51,P2L2	2yrs DM	4.8x3.6x2.6	10	16.65	26
93.	Lakshmi 17841	48,P4L4	2yrs	4.9x3.4x2.4	11	12.4	30
94.	Sivakami 15941	47,P4L3	1yrs	4.1x3.6x2.1	7	10.2	22

95.	Sridevi 16491	48,P4L3	6yrs back HT	4.5x4.2x2.0	6	14.2	26
96.	Tamil Selvi 17941	50,P4L4	4yrs	6.2x4.2x2.0	16	15.62	24
97.	Chitra 14981	48,P4L4	6yrs DM	6.1x3.2x2.1	8	32.2	21
98.	Visalatchi 17894	50,P2L2	4yrs DM	5.4x4.2x2.6	16	7.9	23
99.	Meenakshi 17149	47,P3L3	2yrs	5.0x3.4x2.6	8	8.6	27
100.	Sivakami Mariappan 18941	48,P6L6	2 yrs DM	8.4x6.2x2.4	8	11.5	21
101.	B. Eashwari 67238	60 P6L6	1yrs HT	4.3x2.7x1.2	1.2	10.6	30
102.	R. Shanthi 67250	50 P3L3	1yrs	5x2.2x1.4	6	14.6	28
103.	S. Kumari 67252	65 P4L4	8yrs	5x3.8x2.2	14	34.2	22
104.	M. Anjalai 67341	70 P4L4	3yrs DM	4.1x2.7x1.1	3	16	23
105.	A. Ganga 67341	67 P2L2	1yrs DM	3.6x2.9x1.4	4	8.8	25
106.	R. Pappa 67359	73 P4L4	2yrs	3.9x1.8x1.6	5	11.4	31
107.	K. Sumathi 67378	60 P4L4	2yrs HT	4.0x2.0x1.4	4	17.8	26
108.	M.Khursheedbegum 67508	55 P6L6	11/2yrs DM	4.4x2.0x1.1	3	32.6	24
109.	Threseammal 67489	60 P2L2	3yrs DM	3.9x2.0x1.6	5	16.6	26
110.	S.Mallika 67488	59 P3L3	4yrs DM	4.8x2.3x1.1	5	7.8	21

111.	P.Dhanam 67520	54 P4L4	2yrs back HT	6.3x5.3x4.2	16	14.4	24
112.	R.Kasturi 67623	50,P8L8	2yrs	5x3.2x2.4	10	12.2	27
113.	M.Deivanai 67563	50,P7L7	3yrs HT	6.4x3.2x3.4	6	12.6	25
114.	K.Nagamma 67856	44,P2L2	2yrs DM	5.2x2.3x1.1	4	14.4	22
115.	Sheela 67756	54,P5L5	4yrs	4.8x2.8x1.2	5	16.2	28
116.	Rajalshmi 67823	42,P3L3	3yrs	4.6x2.1x1.3	5	17	24
117.	S.Govindammal 67420	60 P6L6	3yrs DM	4.0x2.5x1.4	5	12.6	21
118.	M.Delli 67752	50 P3L3	4yrs HT	6.4x2.3x1.1	10	15.6	23
119.	Bangajammal 67632	65 P4L4	4yrs	5.4x3.0x2.9	8	18.9	23
120.	Kamatchi 5623	70 P4L4	4yrs DM	4.1x1.1x2.1	5	12.6	21
121.	Lakshmi 4569	67 P2L2	2yrs HT	4.6x2.1x1.9	8	12.4	32
122.	L.Palaniyammal 56321	73 P4L4	10yrs	3.6x2.5x1.6	4	17.2	26
123.	Sridevi.R 56987		4yrs	5.2x3.0x2.6	8	18	24
124.	Saratha 86523	60 P6L6	9yrs HT	4.6x2.1x1.1	4	32.2	20
125.	P.Mary 59624	50 P3L3	2yrs	4.8x3.1x2.6	11	14.32	28
126.	M.Maheshwari 45632	65 P4L4	2yrs DM	4.3x2.7x1.2	1.2	16.2	27

127.	P. Rajkumar 45328	70 P4L4	12yrs back HT	5x2.2x1.4	6	15.25	31
128.	S. Chandra 8562	67 P2L2	11yrs	5x3.8x2.2	14	16	25
129.	R. Rajathi 95632	73 P4L4	8yrs	4.1x2.7x1.1	3	12.5	22
130.	K. Shantha 84512	60 P4L4	7yrs DM	3.6x2.9x1.4	4	11.6	24
131.	Bhanumathy 11990	48,P2L2	8yrs	3.9x1.8x1.6	5	14.2	27
132.	Ranikutty 11501	48,P3L3	2yrs	4.0x2.0x1.4	4	27.8	26
133.	Kamala 6869	60,Nullipara	30yrs DM	4.4x2.0x1.1	3	10.25	21
134.	Muniamma 9497	54,P2L2	4yrs HT	3.9x2.0x1.6	5	12.5	25
135.	Rakayee 21865	49,P3L3	6yrs	4.8x2.3x1.1	5	28.6	30
136.	Shanthi 23793	52,P4L3	2yrs	6.3x5.3x4.2	16	11.26	25
137.	Kathammal 13897	50,P6L6	2yrs	5x3.2x2.4	10	14.4	26
138.	Selvi 14901	49,P5L4	6yrs HT	6.4x3.2x3.4	6	14.8	28
139.	Sundari 13741	50,P2L1	6yrs	5.2x2.3x1.1	4	30.24	23
140.	Karupayee 8498	49,P4L2	10yrs DM	4.8x2.8x1.2	5	30.1	20
141.	Senthil 9430	49,P3L2	2yrs DM	4.6x2.1x1.3	5	15	24
142.	Sivapayee 16981	48,P2L3	2yrs	4.0x2.5x1.4	5	12.2	26

143.	Kalairasi 17914	49,P3L1	1yr back DM	6.4x2.3x1.1	10	38.4	30
144.	Laxmi Elumalai 7937	50,P6L6	6yrs DM	5.4x3.0x2.9	8	30.4	22
145.	Bhanumathy 11990	48,P2L2	4yrs	4.1x1.1x2.1	5	10.9	26
146 .	Kanchana 6990	48,P3L3	6yrs	4.6x2.1x1.9	8	10.6	24
147	Kamala 6779	52, P4L3	4yrs DM	4.2x1.2x2.0	4	31.6	25
148.	Vellammal 7938	75,P3L3	2yrs	4.3x2.7x1.2	1.2	9.6	23
149.	Alamelu 11458	54,P2L2	2yrs	5x2.2x1.4	6	9.1	27
150.	Rathinam 11463	60,P4L4	2 yrs DM	5x3.8x2.2	14	32.4	21